

1. A flavivirus comprising a hinge region mutation that attenuates the flavivirus.
2. The flavivirus of claim 1, wherein the mutation decreases the viscerotropism of the flavivirus.
3. The flavivirus of claim 1, wherein the flavivirus comprises a yellow fever virus vaccine strain.
4. The flavivirus of claim 1, wherein the flavivirus is a viscerotropic flavivirus selected from the group consisting of Dengue virus, West Nile virus, Wesselsbron virus, Kyasanur Forest Disease virus, and Omsk Hemorrhagic fever virus.
5. The flavivirus of claim 1, wherein the flavivirus is a chimeric flavivirus.
6. The flavivirus of claim 5, wherein the chimeric flavivirus comprises the capsid and non-structural proteins of a first flavivirus virus and the pre-membrane and envelope proteins of a second flavivirus comprising an envelope protein mutation that attenuates the chimeric flavivirus.
7. The flavivirus of claim 6, wherein the second flavivirus is a Japanese encephalitis virus.
8. The flavivirus of claim 6, wherein the second flavivirus is a Dengue virus.
9. The flavivirus of claim 8, wherein the Dengue virus is Dengue-1, Dengue-2, Dengue-3, or Dengue-4 virus.
10. The flavivirus of claim 1, wherein the mutation is in the hydrophobic pocket of the hinge region of the envelope protein.

11. The flavivirus of claim 10, wherein the second flavivirus is a Dengue virus and the mutation is in the lysine at Dengue envelope amino acid position 202 or 204.
12. The flavivirus of claim 11, wherein the mutation is a substitution of the lysine.
13. The flavivirus of claim 12, wherein the lysine is substituted with arginine.
14. A vaccine composition comprising the flavivirus of claim 1 and a pharmaceutically acceptable carrier or diluent.
15. A method of inducing an immune response to a flavivirus in a patient, the method comprising administering to the patient the vaccine composition of claim 14.
16. The method of claim 15, wherein the patient does not have, but is at risk of developing, infection by the flavivirus.
17. The method of claim 15, wherein the patient is infected by the flavivirus.
18. A method of producing a vaccine comprising a flavivirus, the method comprising introducing into the flavivirus a mutation that results in decreased viscerotropism.
19. The method of claim 18, wherein the mutation is in the hinge region of the envelope protein of the flavivirus.
20. The method of claim 19, wherein the mutation is in the hydrophobic pocket of the envelope protein of the flavivirus.
21. A method of identifying a flavivirus vaccine candidate, the method comprising the steps of:
introducing a mutation into the hinge region of the flavivirus; and

determining whether the flavivirus comprising the hinge region mutation has decreased viscerotropism, as compared with a flavivirus virus lacking the mutation.

22. The method of claim 21, wherein the mutation is in the hinge region of the envelope protein of the flavivirus.

23. The method of claim 21, wherein the flavivirus is a yellow fever virus.

24. The method of claim 21, wherein the flavivirus is a chimeric flavivirus.

FLAVIVIRUS VACCINES

The invention provides attenuated flavivirus vaccines and methods of making and using these vaccines.